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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/833,017	04/10/2001	Dennis Cvitkovitch	1889-00401	8365

23505 7590 12/13/2002

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EXAMINER	
BASKAR, PADMAVATHI	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 12/13/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/833,017	CVITKOVITCH ET AL.	
	Examiner	Art Unit	
	Padmavathi v Baskar	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspond nce address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 September 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6 and 22-33* is/are pending in the application.

4a) Of the above claim(s) *6 and 29-31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,22-28,32 and 33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *11* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicant's amendment filed on 7/16/02 (paper No 12) and 9/13/02 (paper #15) is acknowledged. Claims 1-6, 22-33 are pending in the application.

Priority

2. Acknowledgment is made of applicant's claim for applications CANADA 2,302,861 04/10/2000 and CANADA 2,332,733 02/20/2001 foreign priority under 35 U.S.C. 119(a)(d). However, the certified copies of CANADA 2,302,861 04/10/2000 and CANADA 2,332,733 02/20/2001 have not been received by the office. Applicant is advised to submit the certified copies of patent CANADA 2,302,861 and CANADA 2,332,733. Applicant's claim for provisional application 60/269,949 02/20/2001 domestic priority under 35 U.S.C. 119(e) acknowledged and priority is granted as of 2/20/01.

Drawings

3. The drawings are not accepted by the draftsperson under 37 C.F.R. 1.84 or 1.152. Applicant should comply with the objections to the drawings as set forth in Form- 948 (Draftsperson's Notice) mailed with this Office action.

Information Disclosure Statement

4. Information Disclosure Statement filed on 7/8/02 (Paper # 11) is acknowledged and a signed copy is attached to this Office action.

Election

5. Applicant's election of Group I claims 1-5, 22-28, 32-33 with respect to SEQ.ID.NO: 2 and 4 in Paper No 12 (7/16/02) without traverse is acknowledged. Applicant's request the examiner to examine claims 1-5, 22-28, 32-33 with respect to SEQ.ID.NO: 2 and 4 since

SEQ.ID.NO: 4 is a part of SEQ.ID.NO: 2. The Examiner has withdrawn the restriction requirement between SEQ.ID.NO: 2 or 4 and will examine claims 1-5, 22-28, 32-33 with respect to SEQ.ID.NO: 2 and 4. Claims 6 and 29-31 have been withdrawn from consideration. Claims 1-5, 22-28, 32-33 are under examination.

Claim Rejections - 35 USC 112, first paragraph

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claim 1 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.
Applicant is referred to the interim guidelines on written description published June 15, 1998 in the Federal Register at Volume 63, Number 114, and pp 32639-32645 and also available at www.uspto.gov/web/tws/b3b.teachthrough.pdf

Claim 1 is drawn to a compound that competitively inhibits binding of CSP to S.mutans histidine kinase. However, the specification discloses only polypeptides, SEQ ID N0 2 and 4 inhibit binding of CSP to S.mutans histidine kinase. A compound that competitively inhibits binding of CSP to S.mutans histidine kinase would include many species of inhibitors such as antibiotics, antibodies that bind to surface antigens ComC, D and E s, peptide precursor from ComC, D and E, tooth paste, mouthwash, food and food additives etc. In analyzing whether the written description requirement is met for genus claim, it is first determined whether a

representative number of species of compounds have been described by their complete structure. In the instant case, SEQ ID N0 2 and 4 are the only species whose complete structure is disclosed. Therefore, this limited information disclosed in the specification is not deemed sufficient to reasonably convey to one skilled in the art that Applicant is in possession of a compound that competitively inhibits binding of CSP to S.mutans histidine kinase at the time the application was filed. Thus it is concluded that the written description requirement is not satisfied for the claimed genus.

8. Claims 1, 5, 22-28 and 32-33 (as a vaccine composition only) are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims are drawn to a pharmaceutical composition or vaccine composition comprising compounds that competitively inhibit binding of CSP (competence signal peptide) to S.mutans histidine. Compound is a peptide or an antibody. Enablement of a "pharmaceutical composition" or "vaccine" is considered to rest on a teaching of in vivo administration for purposes consistent with the intended use disclosed in the specification. The disclosed intended use for the claimed pharmaceutical compositions/vaccine is for the treatment of dental caries. Thus, the nature of the invention is a therapeutic composition used in the treatment of dental caries caused by S.mutans.

Although the specification discloses the claimed composition, and general methods for formulating compositions in pharmaceutically acceptable carriers, there is insufficient guidance which would enable one skilled in the art to use the claimed compositions for their intended purpose, viz., for the generation of a protective immune response against dental caries

At the time the invention was made vaccines comprising the claimed products, SEQ.ID.NO: 2 or 4 (i.e., in vivo) were not routinely used and is unpredictable since the art recognizes that in vitro activity does not correlate with in vivo efficacy.

(1) The compound/peptide may be inactivated before producing a sufficient effect, e.g. such as proteolytic degradation, immunological inactivation

(2) The compound may have poor bioavailability (e.g. may be adsorbed or absorbed by fluid), and

(3) A large enough effective local concentration may not be capable of being established even with administration of excess amounts, particularly as such relates to ensuring that adverse side effects do not occur that would prohibit use of such compound in therapy. See M.P.E.P. 608.01(P) and Ex parte Aggarwal, 23 USPQ2d 1334 1337 1338 (BPAI 1992). Benet *et al.*, 1990, in The Pharmacological Basis of Therapeutics, Gilman et al., eds. Pergamon Press, New York, pp. 3-32. The specification lacks guidance by way of general methods or working examples, which teach an "effective amount" of peptide, or antibody, which would be used for this purpose. Lack of working examples is given added weight in cases involving an unpredictable and undeveloped art, such as immunotherapy of dental caries. It is unpredictable whether the claimed pharmaceutical composition, which is disclosed as being immunogenic, would have the added property of generating an immune response sufficient to inhibit dental caries, because the specification has not disclosed a link or nexus between the generation of protective immunity and its use in preventing dental caries. Further, it is not routine in the art of immuno therapy to use compositions analogous to the claimed compositions for this purpose. Accordingly, there is no objective basis upon which the skilled artisan would reasonably be able to determine or predict an amount of the claimed composition/vaccine effective for its intended use. Therefore, undue experimentation would be required to make and use the invention.

8. Claims 1-5 22-28 and 32-33 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a compound comprising SEQ.ID.NO 2 or 4 does not reasonably provide enablement for a compound comprising fragments of SEQ.ID.NO 2 or 4 or derivatives of fragments SEQ.ID.NO 2 or 4 or parts of amino acid sequences of SEQ.ID.NO: 2 or 4 or sequences having 30%, 50% or 60%. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification is enabled for compound comprising SEQ.ID.NO 2 or 4 does not reasonably provide enablement for a compound comprising fragments of SEQ.ID.NO 2 or 4 or derivatives of fragments SEQ.ID.NO 2 or 4 or parts of amino acid sequences of SEQ.ID.NO: 2 or 4 or a sequences having 30%, 50% or 60%. It is unclear to one skilled in the art what sequences are embraced by the claim since the specification lacks the algorithm and parameters used to determine percent identity or derivatives of fragments. If it is unclear to one skilled in the art what sequences are embraced by a claim which is based on a specification which lacks the algorithm and parameters used to determine percent homology/identity/similarity, the specification is non-enabling, since one skilled in the art would not be able to make and use those sequences without undue experimentation.

Additionally, it is noted that applicants have listed fragments of SEQ.ID.NO 2 or 4 or derivatives of fragments SEQ.ID.NO 2 or 4 or parts of amino acid sequences of SEQ.ID.NO: 2 or 4. It is well known that for proteins, for example, even a single amino acid change can destroy the function of the biomolecule. The effects of these changes are largely unpredictable as to which ones have a significant effect versus not. Further, specification is silent on how to make these proteins with sequence identity to SEQ.ID.NO: 2 or 4. What changes would have an adverse effect on the function of this peptide is not predictable. It is known in the art that

derivatives or variants, which are obtained by substitutions, deletions, or modifications of the amino acids of a protein, alter the function of the protein. The amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and still retain similar activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expected intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, the problem of predicting protein structure from mere sequence data of a single protein and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein and finally what changes can be tolerated with respect thereto is extremely complex (Bowie et al. Science, Vol. 247: 1990; p. 1306; p. 1308) and is well outside the realm of routine experimentation. Applicant failed to give direction on what fragments of SEQ.ID.NO 2 or 4 or derivatives of fragments SEQ.ID.NO 2 or 4 or parts of amino acid sequences of SEQ.ID.NO: 2 or 4 would be suitable in order to elicit the desired protective immune response as a vaccine. Therefore, the claimed fragments result in an unpredictable biomolecule without any function.

Claim Rejections - 35 USC 112, second paragraph

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

10. Claims1-5, 22-28 and 32 and rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-5 are indefinite because they contain the abbreviations "CSP" etc. Full terminology should be in each instance in the claims without the additional use of redundant abbreviations in parentheses or otherwise. Correction is required.

It is not clear what are the metes and bounds of "competitively." As written, it is difficult to determine the metes and bound of competitively inhibits binding of CSP to S.mutans histidine kinase.

Claim 4 recites the limitation "amino acids" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim 5 recites the limitation "polypeptide" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim 3 is rejected as being vague in reciting "derivative". It is not clear what is a derivative of an antibody?

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 1-5, 22-28 and 32-33 are rejected under 35 U.S.C. 102(b) as being anticipated by Russel 1985 ((U.S.Patent 4,521,513).

Claims are directed to a compound that inhibits binding of CSP to S.mutans hisidine and pharmaceutical composition and vaccine comprising the same. Claims are also directed to an

isolated CSP or fragment comprising S.mutans CSP activity.

Examiner is viewing the claims that recite a compound that inhibits binding of CSP to S.mutans as cell wall antigens.

Russel discloses an isolated antigenic protein C, present in the cell walls of S.mutans which reads on the compound that inhibits the binding of CSP to S.mutans histidine because the prior art protein (i.e., antigen or competent signal peptide) is extracted from competent bacteria S.mutans, Inbritt strain and is used to prevent dental caries from bacteria S.mutans (see column 4, lines12- 46). Further, the prior art discloses monkeys were protected from caries (see figure2 and column 7, lines 23-32). The antigenic protein C reads on an isolated CSP because protein c is isolated from S.mutans cell wall antigens that inherently comprise the CSP peptide since the antigen is prepared from widely known competent strain of Inbritt strain. This antigenic protein comprises amino acid sequences of SEQ.ID.NO 2 or 4. . Characteristics such as amino acid sequence would be inherent in the preparations of Russel. Examiner is viewing the claims as having open claim language (i.e., comprising) Applicant's use of the open-ended term "comprising " in claims fails to include unrecited steps or ingredients and leaves the claims open for inclusion of unspecified ingredients, even in major amounts). See In re Horvitz, 168 F 2d 522, 78 U.S.P.Q. 79 (C.C.P.A. 1948) and Ex parte Davis et al., 80 U.S.P.Q. 448 (PTO d. App. 1948). In the absence of evidence to the contrary the disclosed prior art composition and the claimed composition are the same. Since the Office does not have the facilities for examining and comparing applicants' claimed composition with the composition of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed composition and the composition of the prior art. It is acknowledged that weight is given to every term in claims. This is why the instant claims drawn to pharmaceutical compositions and vaccine are scrutinized differently from a composition claim under 112, first paragraph. However, under prior art rejections, the term pharmaceutical compositions must be weighed with the structural limitations of the claim. If the pharmaceutical compositions merely comprise a known composition, the term carries little weight absent evidence of structural difference. Of course, the existence of an unobvious structural difference would define over the prior art. Here, the prior art teaches the same compound, peptide as claimed.

In re Thorpe, 227 U.S.P.Q. 964, 966 (Fed. Cir. 1985). In re Marosi, 218 U.S.P.Q. 289, 293-293 (C.A.F.C. 1983). In re Best, 195 U.S.P.Q. 430, 433 (C.C.P.A. 1977). In re Brown, 173 U.S.P.Q. 685, 688 (C.C.P.A. 1972).

13. Claims 1-5 and 32 are rejected under 35 U.S.C. 102(b) as being anticipated by Taubman et al 1979(U.S.Patent 4,150,116).

Claims are directed to a compound that inhibits binding of CSP to S.mutans and an isolated CSP comprising SEQ.ID.NO: 2 or 4, pharmaceutical or vaccine compositions comprising the same.

Taubman et al disclose a glucosyl transferase (see columns 4-5 and claims) obtained from S.mutans, which is a cariogenic bacteria and is resistant to streptomycin (i.e., CSP). Characteristics such as amino acid sequence would be inherent in the preparations of Taubman et al. Examiner is viewing the claims as having open claim language (i.e., comprising) Applicant's use of the open-ended term "comprising " in claims fails to include unrecited steps or ingredients and leaves the claims open for inclusion of unspecified ingredients, even in major amounts). See In re Horvitz, 168 F 2d 522, 78 U.S.P.Q. 79 (C.C.P.A. 1948) and Ex parte Davis et al., 80 U.S.P.Q. 448 (PTO d. App. 1948). In the absence of evidence to the contrary the disclosed prior art composition and the claimed composition are the same. Since the Office does not have the facilities for examining and comparing applicants' claimed composition with the composition of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed composition and the composition of the prior art. It is acknowledged that weight is given to every term in claims. This is why the instant claims drawn to vaccines or pharmaceutical compositions are scrutinized differently from a composition claim under 112, first paragraph. However, under prior art rejections, the term vaccine must be weighed with the structural limitations of the claim. If the vaccine merely comprises a known composition, the term carries little weight absent evidence of structural difference. Of course, the existence of an unobvious structural difference would define over the prior art. Here, the prior art teaches the same compound, peptide as claimed.

In re Thorpe, 227 U.S.P.Q. 964, 966 (Fed. Cir. 1985). In re Marosi, 218 U.S.P.Q. 289, 293-293 (C.A.F.C. 1983). In re Best, 195 U.S.P.Q. 430, 433 (C.C.P.A. 1977). In re Brown, 173 U.S.P.Q. 685, 688 (C.C.P.A. 1972).

14. Claims 1-2 and 5 are rejected under 35 U.S.C. 102(b) as being anticipated by Gristina et al 1996 (U.S.Patent 5,530,102).

Claims are directed to a compound that inhibits binding of CSP to S.mutans hisidine Examiner is viewing these claims to recite a compound that inhibits binding of CSP to S.mutans

as antibodies that inhibit the binding of S.mutans (claims 1-5) since this antibody is specific and inhibits S.mutans.

Gristina et al disclose an antibody specific for S.mutans (see column 13, lines 2-5 and claims 6 and 7). The prior art teaches pharmaceutical composition comprising antibodies that inhibit binding of CSP to S.mutans in various carriers such as crème, ointments and lavage fluids etc (see column 5, lines 14-39). The antibody of Gristina et al is the same as the compound of the instant invention. In the absence of evidence to the contrary, the claimed invention is same as the prior art product. Since the Office does not have the facilities for examining and comparing applicant's product and the product of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art. It is acknowledged that weight is given to every term in claims. This is why the instant claims drawn to pharmaceutical compositions are scrutinized differently from a composition claim under 112, first paragraph. However, under prior art rejections, the term pharmaceutical compositions must be weighed with the structural limitations of the claim. If the pharmaceutical compositions merely comprise a known composition, the term carries little weight absent evidence of structural difference. Of course, the existence of an unobvious structural difference would define over the prior art. Here, the prior art teaches the same compound, peptide as claimed.

In re Thorpe, 227 U.S.P.Q. 964, 966 (Fed. Cir. 1985). In re Marosi, 218 U.S.P.Q. 289, 293-293 (C.A.F.C. 1983). In re Best, 195 U.S.P.Q. 430, 433 (C.C.P.A. 1977). In re Brown, 173 U.S.P.Q. 685, 688 (C.C.P.A. 1972).

15. Claims 1-2 and 5 are rejected under 35 U.S.C. 102(b) as being anticipated by Lehner et al 2000 (U.S.Patent 5,530,102).

Claims are directed to a compound that inhibits binding of CSP to S.mutans hisidine Kinale. Examiner is viewing these claims to recite a compound that inhibits binding of CSP to S.mutans as antibodies that inhibit the binding of S.mutans (claims 1-5) since this antibody is specific and inhibits S.mutans

Lehner et al disclose polypeptide fragments capable of competition with S.mutans (see abstract and claims) antigen I/II. The prior art teaches pharmaceutical composition comprising these peptides in pharmaceutically acceptable carrier that inhibit or prevent carriers by eliciting

an immune response (see claims 22-24) The antibody of Gristina et al is the same as the compound of the instant invention. In the absence of evidence to the contrary, the claimed invention is same as the prior art product. Since the Office does not have the facilities for examining and comparing applicant's product and the product of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art. It is acknowledged that weight is given to every term in claims. This is why the instant claims drawn to pharmaceutical compositions are scrutinized differently from a composition claim under 112, first paragraph. However, under prior art rejections, the term pharmaceutical compositions must be weighed with the structural limitations of the claim. If the pharmaceutical compositions merely comprise a known composition, the term carries little weight absent evidence of structural difference. Of course, the existence of an unobvious structural difference would define over the prior art. Here, the prior art teaches the same compound, peptide as claimed.

In re Thorpe, 227 U.S.P.Q. 964, 966 (Fed. Cir. 1985). In re Marosi, 218 U.S.P.Q. 289, 293-293 (C.A.F.C. 1983). In re Best, 195 U.S.P.Q. 430, 433 (C.C.P.A. 1977). In re Brown, 173 U.S.P.Q. 685, 688 (C.C.P.A. 1972).

Status of Claims

15. No claims are allowed.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Padma Baskar whose telephone number is (703) 308-8886. The examiner can normally be reached on Monday through Friday from 6:30 AM to 4 PM EST

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (703) 308-3909. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Padma Baskar Ph.D

11/17/02.

LYNETTE F. SMITH
PRIMARY EXAMINER
GROUP 1800